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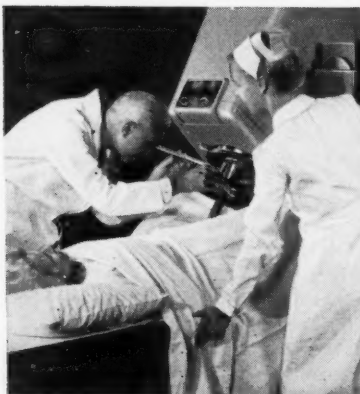
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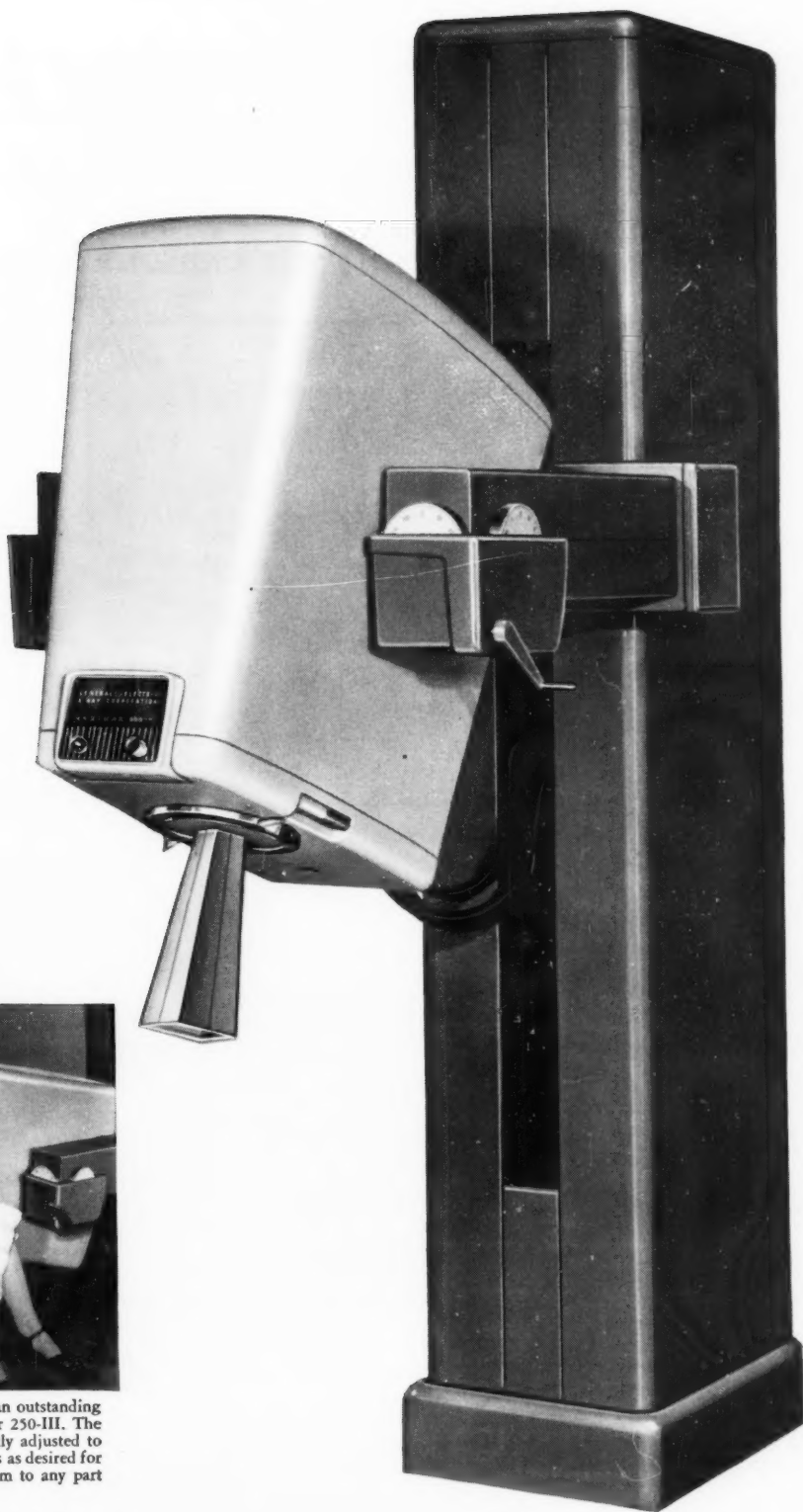
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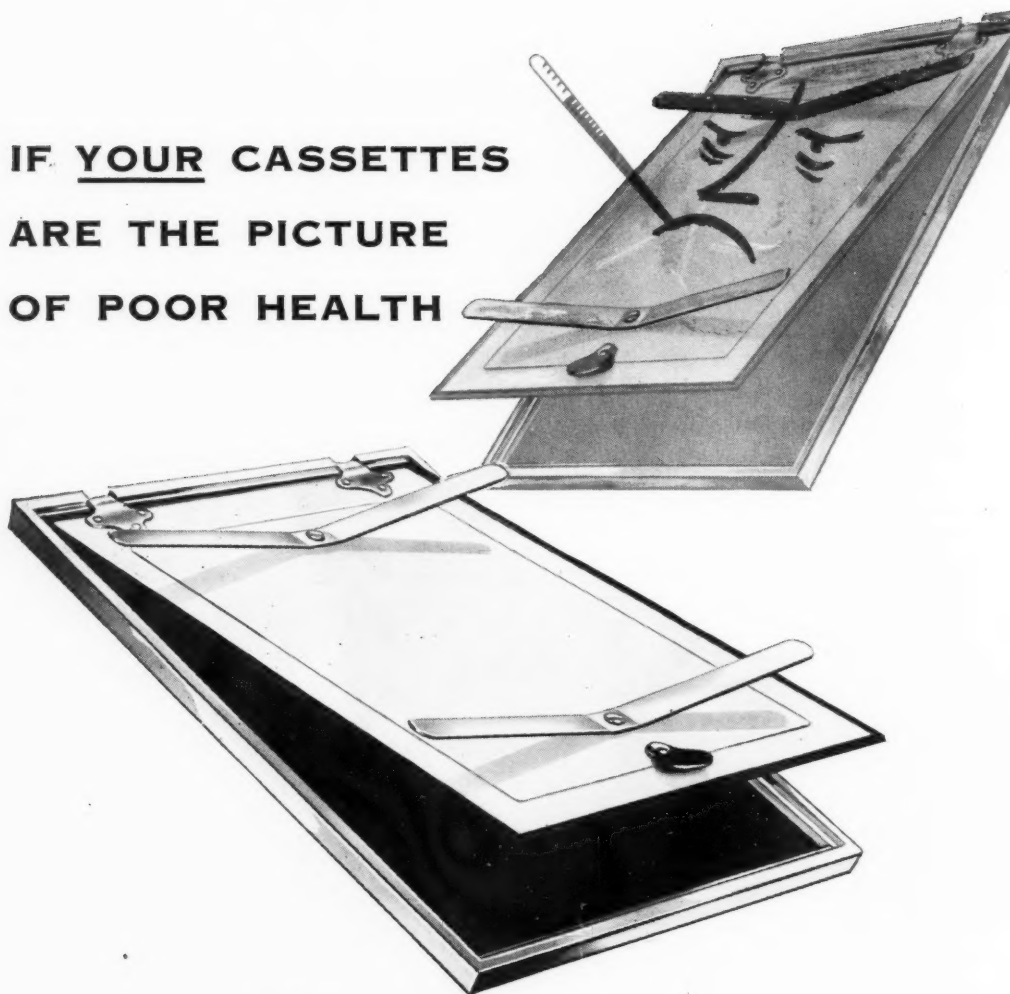
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RADIATION LEUKOPENIA AND CORTISONE

CHAS. C. BURKELL, M.D., D.M.R.T.

Assistant Director

SASKATOON CANCER CLINIC
Saskatoon, Saskatchewan

Whenever large fields are used in the x-ray treatment of malignant tumors, the depression of the hemopoietic system often prevents an adequate tumor dose being achieved. Any method which would prevent or overcome this depression would be a useful therapeutic agent in the hands of the radiotherapist.

Introduction

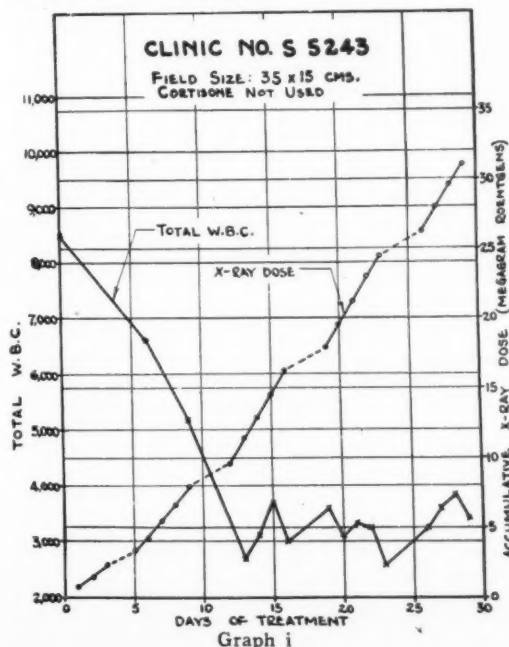
Pearson and his associates⁵ have reported a rise in the leukocyte counts, in cases of leukemia, during administration of cortisone and ACTH even though there was regression of lymphoid tumors. Wintrobe⁷ noted stimulation of the granulopoietic tissue as manifested by the development of neutrophilic leukocytosis in 13 of 16 patients. Caldwell et al² reported the successful treatment of a patient with cortisone who had severe agranulocytosis. Radiation sickness, which is often associated with hemopoietic depression, has been benefited by cortisone, as reported by Ellinger, Roswit and Glasser³. Bethel¹ reports two cases of splenic neutropenia in which the neutropenia was corrected after the administration of ACTH for six and ten days respectively.

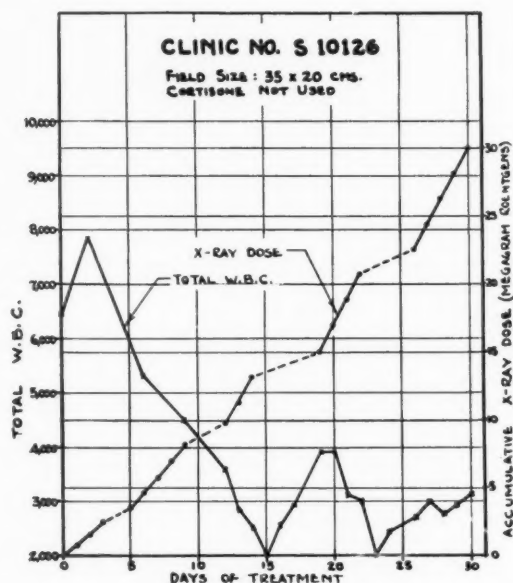
In view of the results of these investigations, cortisone was therefore given to six patients undergoing large field abdominal irradiation therapy. Two additional patients were given cortisone after their leukocyte count had fallen to a dangerously low level. The following is a discussion of the results.

Four patients, who received large field abdominal irradiation therapy, without cortisone, were a "control" series.

The radiotherapeutic technique was the same in both the "control" and "cortisone" groups of patients. Large fields, employing the trunk-bridge technique as developed at Manchester⁴, were used in all cases. The size of the fields varied whether the aim was to include the entire peritoneal cavity or just the para-aortic and iliac nodes in the irradiated zone. Consequently the fields varied in size from 35 x 15 to 35 x 20 cms. Treatment was started in each case by giving a dose of

35 r to each of the four fields. The dose was then increased by 5 r daily to each field until a maximum of 85 - 100 r was being administered. The overall time of treatment was approximately five weeks. A tumor dose of 2,500 r was the aim in all cases, but the integral dose, upon which the depression of the hemopoietic system is largely dependent, varied greatly from one patient to another. This figure varied with the different thicknesses of the patients treated. The integral dose was calculated, taking into account the size of the fields, the volume of tissue irradiated, and the technical factors employed in the irradiation. Dr. H. E. Johns and his associates were responsible for the mathematical work and, although the figures given may not represent the exact accumulated megagram roentgens, the method of calculation was the same in each case so that any error is constant, and results are comparable.





Graph ii

Control Group of Patients

Graphs i and ii illustrate the expected behavior of the leukocyte count when large field irradiation therapy, without cortisone, is given to a patient. These are typical examples of the control series of cases. It will be seen there is a fairly rapid and steady decline of the white blood cell count to a total level of approximately 2,000 per cu. mm., occurring usually between the 10th and 15th day of treatment. The total number of leukocytes then levels off with variations between 2,000 and 3,000 white blood cells per cu. mm. until the completion of treatment. In some cases further depression occurs necessitating cessation of treatment either temporarily or permanently because of the danger of severe leukopenia or subsequent aplastic anemia developing.

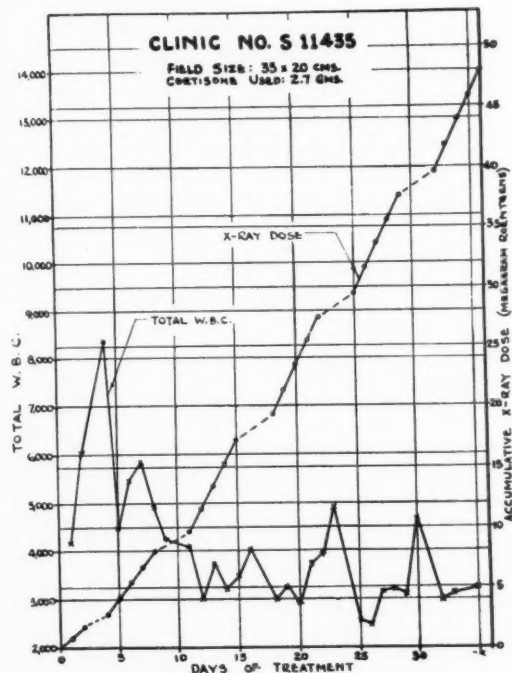
Of the four patients in the control series, two had serous cystadenocarcinoma of the ovary with peritoneal implants, one had bilateral pseudomucinous cystadenocarcinoma of the ovary with omental spread and ascites, and the fourth patient had lymphosarcoma of the stomach with possible involvement of the retrogastric lymph nodes. In each patient the number of white blood cells in the peripheral blood rapidly fell to a count varying from 1,950 - 2,750 white blood cells per cu. mm. This fall occurred over the first twelve or thirteen days after commencement of treatment. With this fall in the total number of white blood cells, all the white blood cell elements were

affected. In no case was the fall of the combined lymphocyte and monocyte count below 300 mononuclear cells per cu. mm. This level is taken as indicating the need to proceed with care should further radiation be given⁵. Three patients had nausea and vomiting of varying severity and one had neither. In two patients the nausea and vomiting subsided after the first week of treatment.

Cortisone Supported Group of Patients

There were six patients in the group to whom cortisone was administered during their radiation therapy. The cortisone was given in a single daily dose of 100 mgms., intramuscularly, only on those days on which the patients received irradiation. The leukocyte count was done on blood taken from the patients shortly after breakfast and before either cortisone or irradiation had been given.

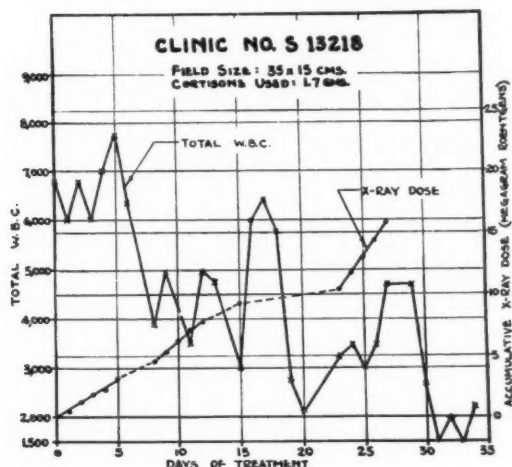
The following is a summary of the patients treated. In each case a graph, illustrating the total white blood cell level and the integral x-ray dose in megarems roentgens, accompanies the description.



Case No. S-11435

This was a female patient aged 58 who had a papillary cystadenocarcinoma of the left ovary with direct extension to the broad ligament and uterus. Large field abdominal irradiation was commenced on January 26th,

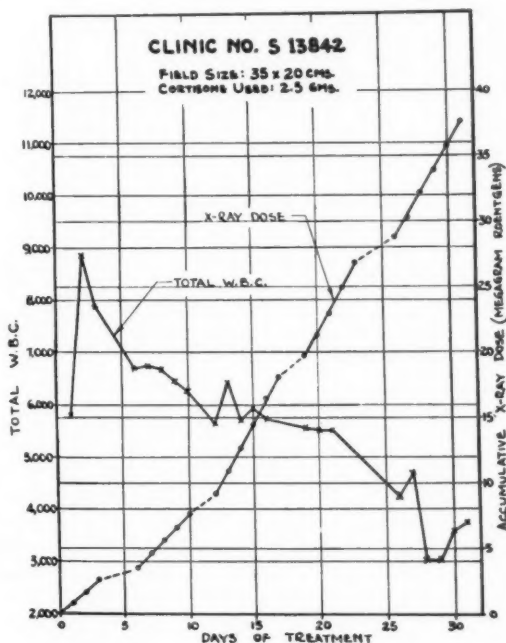
1951 and completed on March 2nd, 1951. Cortisone was administered each day the patient received irradiation therapy. It is seen that there was essentially the same type of curve as with the control group of patients except that the total number of leukocytes fell only to 3,000 cells per cu. mm. The lowest number recorded during the treatment was 2,400 cells per cu. mm. This was on the twenty-fifth day after commencement of treatment. Upon the conclusion of treatment the total number of leukocytes was 3,250 cells per cu. mm. The lowest recorded combined lymphocyte and monocyte count was 325 mononuclear cells per cu. mm. This patient had only mild nausea and vomiting during the first week of treatment.



Case No. S-13218

This was a 47-year-old female patient who had a papillary serous cystadenocarcinoma of both ovaries with peritoneal extension. Large field abdominal irradiation was started on August 14th, 1950, and was discontinued on September 9th, 1950. The accompanying graph shows a general decline in the white blood cell level until the fifteenth day after commencement of treatment. There was a sudden rise on that day. The patient developed a marked pyrexia and complained of a dull pain in her right lumbar area. Her urine contained numerous pus cells. Irradiation therapy and cortisone were discontinued and the patient was given penicillin to combat her pyelitis. Treatment was recommenced on the twenty-third day but again the patient developed pyrexia, lumbar pain, and pyuria. Persistence of treatment was considered inadvisable and was therefore stopped on the twenty-seventh

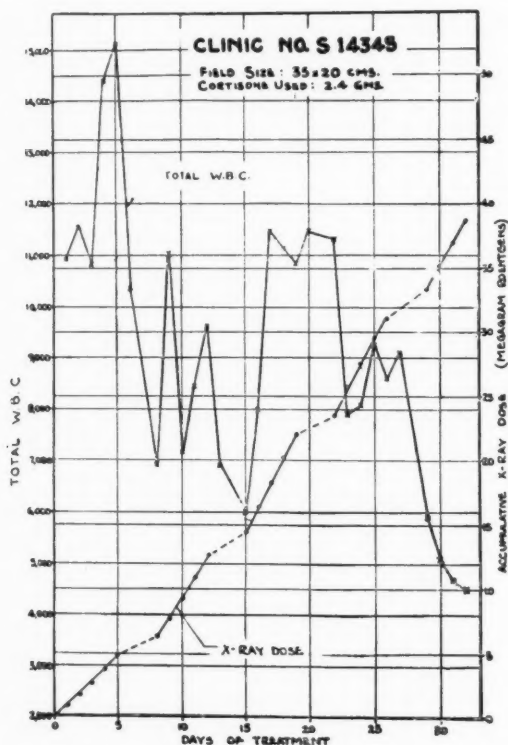
day. She was observed over a further period of seven days and a marked depression of the total white blood cell count was observed even though no irradiation was being given. We do not know if this depression was simply a delayed depression caused by the irradiation which may not have occurred if further cortisone had been given. This patient, too, had slight nausea and vomiting during the early part of her treatment.



Case No. S-13842

This was a 50-year-old female patient who had generalized carcinomatosis peritonei from carcinoma of the ovary (type not specified). Four-field trunk-bridge abdominal irradiation was started on December 28th, 1950, and was completed on January 27th, 1951.

The white blood cell level at no time fell below 3,000 cells per cu. mm. The daily drop was less and the maximum fall did not occur until the twenty-eighth day after commencement of treatment. However, this patient showed a marked depression in the combined lymphocyte and monocyte count. On the twenty-eighth day there were only 120 mononuclear cells per cu. mm. No serious ill effects, however, were suffered by the patient and on completion of treatment there were 518 mononuclear cells per cu. mm. This patient had no nausea and vomiting.



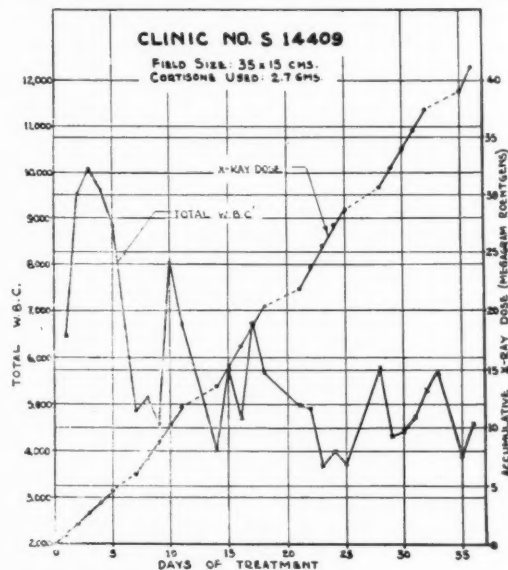
Case No. S-14345

This was a 22-year-old male patient who had lymphosarcoma of the ileum with secondary deposits in the mesentery, peritoneum, and abdominal lymph nodes. Four-field trunk-bridge irradiation to the entire abdomen was given from April 16th to May 17th, 1951. At the commencement of this treatment the white blood cell count was 10,950. During treatment the count showed considerable fluctuation from day to day but for the main part remained within normal range until the end of treatment. The lowest recorded count was 4,500 cells per cu. mm., which occurred on the final day of treatment. The combined lymphocyte and monocyte count was lowest at that time, too, but there were still 630 mononuclear cells per cu. mm.

There have been reported cases of lymphosarcoma in which the lymphosarcomatous masses disappeared with the administration of cortisone alone^{7, 8}. One would expect, therefore, better therapeutic results by combining radiotherapy, which can also cause disappearance of lymphosarcomatous tissue, with cortisone. In this particular patient the disease was apparently unaffected by either therapeutic agent for death occurred on June 2nd, 1951, (sixteen days after completion of treat-

ment) from intestinal obstruction and its sequelae caused by extension of the disease.

During the combined radiation and cortisone therapy the patient had mild nausea and vomiting during the first week of treatment.

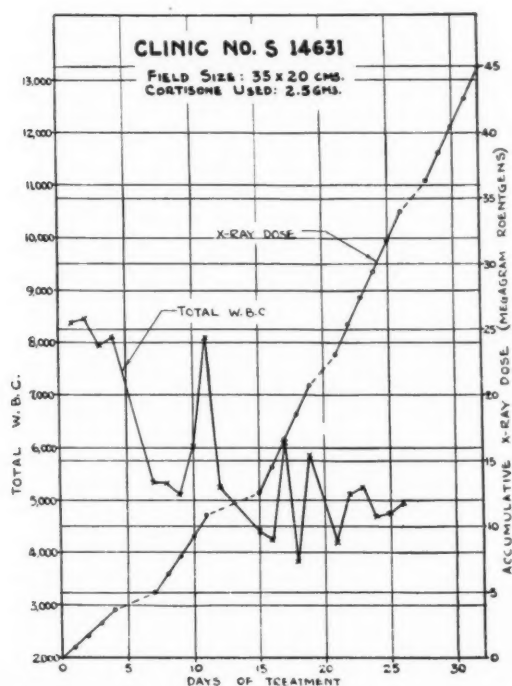


Case No. S-14409

This was a 34-year-old male patient who had a malignant teratoma of the testis. Irradiation of the entire lymphatic drainage system of the testicle, scrotum and spermatic cord was given using the four-field trunk-bridge technique for the para-aortic and iliac nodes and a single field 10 cm. 2 for the right half of the scrotum and the adjacent lymph node area. Treatment was given from April 17th to May 22nd, 1951. At no time did the white blood cell count fall below 3,700 cells per cu. mm. The slope of the curve was much more gradual than with the control cases. The combined lymphocyte and monocyte count was also well maintained. The lowest recorded count was 407 mononuclear cells per cu. mm. This patient, too, had only slight nausea and vomiting during the first week of treatment.

Case No. S-14631

This was a female patient aged 27 years who had a pseudomucinous cyadenocarcinoma of the right ovary. The cyst was ruptured during operative removal with contamination of the peritoneal cavity. Four-field trunk-bridge irradiation was administered from June 19th to July 20th, 1951. The lowest white blood cell count occurred on the seventeenth day. This count was 3,850 cells per cu. mm. On completion of treatment the leukocyte count was 5,100 cells per cu. mm. The lowest com-



bined lymphocyte and monocyte count was 342 mononuclear cells per cu. mm. This patient had mild nausea and vomiting during the first week of treatment. She also had mild depression which disappeared even though the administration of cortisone was continued. The patient felt the depression was due to 'home-sickness'.

Two additional patients who received large-field abdominal irradiation developed leukopenia during treatment. These patients were then given cortisone to determine if it were possible to overcome the leukocyte depression once it had developed.

Case No. S-14560

This was a 71-year-old female patient who had an inoperable carcinoma of the ovary (type not specified). Four-field trunk-bridge irradiation, fields 35 x 15 cms., was given from May 16th to June 20th, 1951. The leukocyte level fell rapidly to a count of 1,850 cells per cu. mm. on the sixteenth day. Cortisone was then given in daily doses of 100 mgms. intramuscularly each day the patient received x-ray treatment. There was a gradual recovery and upon completion of treatment there were 4,150 white blood cells per cu. mm.

Case No. S-13996

This was a 51-year-old male patient who had a seminoma of the right testicle. Four-field trunk-bridge irradiation with an added 15 x 10 cm. field to the right scrotum and

adjacent inguinal area was given from June 19th to February 22nd, 1951. On the thirteenth day after commencement of treatment the leukocyte count was 2,100 per cu. mm. Cortisone, in daily doses of 100 mgms. given intramuscularly, was started. There was a rapid improvement with the leukocyte count being 5,600 cells per cu. mm. at the end of treatment.

Comment

During the combined x-ray and cortisone treatment daily records were kept of the patient's weight, blood pressure, leukocyte count and emotional status. In addition, a weekly record of their complete blood picture, serum proteins, blood urea, and urinalysis was made. The nurses were asked to record the presence or absence of oedema. In no case was there any manifestation of cortisone toxicity. The mild depression exhibited by Case No. S-14631 was most likely unrelated to the cortisone administration.

Conclusions

With the exception of Case No. S-13218, cortisone prevented the leukocyte count from becoming seriously depressed during large-field irradiation treatment. In addition, the depression which did occur became manifest more slowly than in the control series of patients. Two patients, who were given cortisone only after leukocyte depression had occurred showed a prompt recovery of their white blood cell counts even though irradiation treatment was continued. Nausea and vomiting was experienced by nearly all the patients, control as well as cortisone-supported groups, but disappeared during the second week of treatment. The concomitant administration of cortisone seemed to have little or no effect on the prevention of this phase of radiation sickness.

Acknowledgements

1. The cortisone for this study was supplied by the National Research Council under project No. C 99.
2. Dr. H. E. Johns, physicist to the Saskatchewan Cancer Commission, calculated the integral dose on each patient.

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CANADIAN SOCIETY OF RADIOLOGICAL TECHNICIANS

The 10th Annual Convention of the Canadian Society of Radiological Technicians will be held in Calgary at the Hotel Palliser on September 3rd, 4th, 5th and 6th, 1952.

ANNUAL MEETING

The Canadian Association of Radiologists
Toronto — January 14th, 15th, 16th, 1953

Tentative Schedule

Meeting of Executive	9 A.M.	Wednesday
Meeting of Council	2 P.M.	January 14th
Scientific Session	All Day	Thursday January 15th
Annual Dinner and Annual General Meeting	6:30 P.M.	Thursday January 15th
Scientific Session	All Day	Friday January 16th

AN INQUIRY INTO THE EFFECTS OF X-RADIATION UPON THE HEART
FROM MULTIPLE THORACIC BEAMS

E. M. CRAWFORD, M.D., A. D. FRENCH, M.D., R. O. KORNELSEN, M.Sc.
The Department of Radiology, The Queen Elizabeth Hospital of Montreal

Two of our patients, one aged fifty-four and the other aged ninety, died within a few weeks following completion of their courses of X-radiation to intrathoracic malignant tumours. Two such events coming within a short time of one another have raised the question whether the X-radiation received by the heart muscle was partly responsible for death. The first patient had a bronchogenic carcinoma of the left main bronchus and he died with congestive heart failure. The cause of death of the second patient was reported as carcinoma of the oesophagus and general anasarca. Autopsies were not obtained.

Recent developments, both technical and therapeutic, lead us to believe that there will be a greater percentage of patients surviving following radiation of intra-thoracic malignant growths. It would seem, therefore, that we should give consideration to the effect of radiation upon such an important organ as the heart, particularly as many of the patients whom we must treat for intra-thoracic malignant growths are in the fifth and sixth decades of life, and are likely to have some cardiac impairment. When one considers the opinions of radiotherapists, these range between two extremes, namely, that it is always necessary to protect the patient's heart against the action of X-radiation, or that any effect upon the heart is a minor consideration compared to the necessity of getting sufficient radiation to the lesion under treatment.

An inquiry addressed to five cardiologists revealed that none was familiar clinically with the effect of X-radiation upon the heart, for none recalled having dealt with a condition in practice that could be traced directly to the effect of X-radiation upon the heart muscle.

Reviewing some of the recent literature in English on the effect of X-radiation on the heart muscle, we have found little of significance. Most of the recent work has been done in France and Germany, and difficulties of translation have not permitted us to study this. We have been forced, therefore, to fall back on an attempt of our own.

We have attempted to simplify the problem by considering the heart as a pumping machine. When the heart muscle is impaired so that with each contraction the volume of blood pumped out by the ventricles is less

than that normally required to maintain the circulation, and one cannot detect a fall in arterial blood-pressure, it would follow that the rate of the heart must increase in order to maintain the normal blood volume. Should the damage to the heart muscle continue, one would expect a steadily rising heart rate, until the load imposed upon the heart reached the maximum capacity of the heart muscle to do work. When this point is reached, symptoms of fatigue and pain, and signs of dyspnoea, congestion and oedema appear. Should, however, the contractile power of a section of the heart muscle begin to fail, for example one ventricle, congestion would occur in that part of the body whose circulation is immediately affected by that ventricle whose power to contract is failing; thus, congestion would appear in the lungs when the left ventricle is impaired or in the systemic veins when the right ventricle is similarly involved. With an increase in venous pressure, there follows an increase in the amount of blood filling the auricles and ventricles during diastole and then the heart enlarges.

To follow such a cycle of events, it has seemed to us that observations of the heart rate, of the arterial blood-pressure, of the presence of adventitious heart sounds, of cyanosis or pallor, the presence of moist rales at the lung bases, any demonstrable increase in the size of the heart, would be clinical evidence by which we might estimate the degree of heart damage. There remains, of course, the electrocardiogram, and from recent observations it would seem that slight variations of muscle conductivity can be recognized. By repeating the electrocardiographic tracings we should obtain indications of improvement or otherwise. What we have in mind is to establish criteria that will give some assessment of the functioning of the patient's heart before, during and after treatment. Comparison of such data would serve as a basis for later observations as the patient visits the neoplastic clinic for follow up.

What the significance of such observations is we cannot say, but we believe that these observations are of value as illustrated by the following case. A labourer in a sugar refinery, aged fifty-nine, came for treatment of carcinoma of the lower third of the oesophagus, which had been proven by biopsy. The lumen of the oesophagus was very narrow, and the patient was only able to take

fluid food. The filling defect in the barium-filled oesophagus, measured 6 cms. in length on the film. The treatment was planned with eight fields, 4 cms. x 15 cms., four anterior and four posterior. The dose was 200 r (skin dose) per field, and three fields were treated daily. During the course of the treatment his heart rate increased to 100 per minute and, though no fall in blood-pressure was found and the patient stated that he felt well, we decided to discontinue treating through the left anterior fields, following the suggestion of Dr. F. Baclesse, whose technique for X-ray treatment of carcinoma of the oesophagus at the Fondation Curie, Paris, omits left anterior thoracic fields¹. At this time the patient had received 1200 r (skin dose) on six fields and 1400 r over the two right anterior fields. Our dose chart for this patient, when corrected for increased transmission, indicated that the tumour of the oesophagus had received a maximum of 1900 r and a minimum of 1700 r at this time, while the greater part of the heart had received between 600 and 800 r. A small portion adjacent to the oesophagus we estimate received 1900r. Gradually during a period of seven weeks, the heart rate came down from 100 to 69 per minute, and the last electrocardiogram reported a change in the voltage of the T-wave regarded as significant of an improvement of the heart muscle. Such an improvement might be due to better nutrition, for the patient had been taking a full diet that was rich in protein.

In addition to the biological effects of radiation upon the heart, it might be assumed that with a decreasing cardiac out-put, normal tissues might well be deprived of their nutri-

tion, thereby lowering their resistance and increasing the invasive potentiality of a malignant growth. Calculations by a transmission method indicate that the percentage of radiation in the thorax at the site of the lesion is twenty to forty percent higher than the usual depth-dose estimations show. We thus have reason to believe that the biological effect of the radiation entering and absorbed by the heart muscle is greater than we realize. However, any attempt to recognize the effect of radiation upon the heart muscle by clinical means, may be complicated in an elderly person by the effect of an associated disease.

The following routine is carried out before the patient is discharged. Observations are made of the heart-rate, blood pressure, (both arms with patient supine) auscultation of the heart, pallor, cyanosis and oedema, the size of the heart checked by means of an X-ray film of chest (72 ins.), and an electrocardiogram, taken before and after a simple exercise test. These records accompany the patient to the out-patient clinic, where follow-up work is done.

Summary

A preliminary inquiry was begun upon the effect of X-radiation on the heart muscle. As a result a definite procedure was instituted before, during and after treatment of patients with intrathoracic malignant growth through multiple fields.

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PRELIMINARY REPORT ON THE USE OF A NEW CONTRAST
MEDIUM: ANGIOPAC

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This report is presented to draw attention to a new medium for angiography and hepato-splenography. Angiopac is an Ethyl-di-iodo stearate in colloidal suspension, manufactured by l'Union Chimique Belge, in Brussels. The first known report on this substance was read by Professor S. Masy¹ from Louvain at the last Symposium Neuroradiologicum in Rotterdam, September 1949. At this Symposium almost half of the reports dealt with cerebral angiography. On that occasion also, Olle Olsson², from Lund, read a paper on the reactions or damage to the brain due to Diodrast or to drugs of the same group.

At Notre-Dame Hospital approximately 400 cerebral angiograms have been done since June 1948. These angiograms were always done with Diodrast under general anaesthesia with Pentothal until last July when we began to receive occasionally a few ampoules of Angiopac for clinical trial. Since that time we have continued to use Diodrast except for the 23 angiograms we are reporting. We were fortunate not to have had many accidents with Diodrast, contrary to the experience of others. We have had only one serious accident, a complete hemiplegia which lasted a few days followed by a monoparesis (hand) which persisted for some time. This accident occurred to a patient who had previously had cerebro-vascular accidents, due, probably, to arteriosclerosis.

Angiopac thus comes at a time when we are looking for a new medium less likely to cause damage to the brain. Like Thorotrast, it is a colloidal suspension. It is, however, not radioactive. Thorotrast was abandoned because of its radioactivity.

Thomas, Henry and Kaplan³ in a recent article state that the danger of remote accidents caused by the radioactivity of Thorotrast is less serious a problem than the danger of late liver and spleen fibrosis and even perivascular fibrosis (at the site of extra-vascular injection) due to the absence of elimination of Thorotrast. Angiopac being eliminated quite rapidly by the kidney, largely within 24 hours, fibrosis is not likely to occur in the liver and spleen.

Extra-vascular injection is possible, and we do not know yet how long the dye takes to disappear from the soft tissues. We observed

two patients in whom it was still visible 24 days after injection. In a third patient dye was seen 42 days after injection, but some resorption had taken place. Perhaps the use of hyaluronidase would hasten resorption. This point is still unsettled. Diodrast, being in aqueous solution, is rapidly eliminated whether injected inside or outside the vessel.

The dose of one c.c. of Angiopac per kilogram is well tolerated by man. Angiopac is not irritating to the vessel; cerebral angiography can therefore be performed easily and painlessly under local anaesthesia with the cooperation of the patient. Grains of Angiopac are small enough to prevent the danger of embolism. The size of these grains is said to be one-fifth of that of a red blood cell. However, violent agitation of the ampoule or an unskilled aspiration can produce a gaseous suspension capable of entailing air embolism. Our recent cerebral angiograms done with Angiopac compare favourably with those done with Diodrast. It seems that the density of the vascular image is greater, but this is very difficult to decide impartially. We are of the opinion that we can obtain more easily an opacification of smaller vessels. This could be explained by the lack of vascular spasm or irritation at the time of injection, or more likely by the physical state of Angiopac, which permits a delay in the dilution by the circulating blood.

Table 1 presents the important facts on the angiograms done with Angiopac. We have done only one arteriogram of the hand and 22 cerebral angiograms. The age of the patients has varied from 4 to 79 years. Unfortunately in the case of the four year-old child, the vessel was missed and 10 c.c. were injected into the neck. Extra-vascular injection was encountered 7 times, that is to say in about one-third of the cases. The dose injected varied from 10 to 50 c.c. This high percentage of extra-vascular injections was due to a change in the neurosurgical staff, with a new resident and a new interne who were not trained to do percutaneous carotid angiography. This was a regrettable coincidence, and just how much the patients will suffer from this inexperience, we do not know at this time. *We strongly advise against using Angiopac unless one is certain the needle is in the artery.*

ANGIOGRAMS - with - ANGIOPAC

Table 1

NUM-BER	REGION	NAME	AGE	DOSE	FINAL DIAGNOSIS	ANESTHESIA	EXTRA-VASCULAR INJECTION	REACTION DURING	REACTION AFTER INJECTION	OPACIFICATION OF SPLEEN
3178	HAND	C. P.	56	20 c.c.	Aneurysm of the hand	NONE	YES (still visible after 24 days).	NONE		GOOD
5566	BRAIN	L. G.	46	50 c.c.	Aneurysm (carotid, bilateral)	LOCAL	YES	NONE	VOMITING	VERY GOOD
5912	BRAIN	L. F.	21	40 c.c.	Epidural hematoma	GENERAL		NONE		POOR
118440	BRAIN	P. S.	37	20 c.c.	Hemiparesis	GENERAL		NONE		GOOD
5921	BRAIN	G. J. P.	29	10 c.c.	Carotid thrombosis	LOCAL		NONE		
5658	BRAIN	L. P.	18	20 c.c.	Skull metastasis from hypernephroma	GENERAL		NONE		
5609	BRAIN	L. A.	60	20 c.c.	Epi-sub and intra-cerebral hematomas	LOCAL	YES (20 c.c. in neck)	NONE		
5623	BRAIN	G. R.	29	20 c.c.	Arterial spasm	GENERAL	YES (minimal)	NONE	CHILLS	POOR
5424	BRAIN	S. R.	19	30 c.c. (10 to 20 at a week interval)	Skull fracture	GENERAL		NONE	CHILLS after second arteriogram	POOR
4616	BRAIN	L. C.	52	20 c.c.	Internal carotid thrombosis.	GENERAL		NONE	SHOCK - CONVULSIONS (1 hour)	POOR
4630	BRAIN	R. J. E.	?	10 c.c.	Sub-dural hematoma	LOCAL		NONE		
4521	BRAIN	O. G.	53	30 c.c.	Arteriosclerosis	LOCAL	YES (minimal) (still visible after 12 days)	NONE	VOMITING	
4243	BRAIN	A. L.	21	20 c.c.	Migraine ?	LOCAL		NONE		GOOD
4409	BRAIN	N. L. P.	53	40 c.c. (of which 3 amp. no good)		LOCAL		NONE	CHILLS	GOOD
2279	BRAIN	D. A.	79	30 c.c.	Glioblastoma	LOCAL		NONE		
2183	BRAIN	P. E.	36	30 c.c.	Psychoneurosis	LOCAL		NONE	VOMITING - CHILLS	
1342	BRAIN	S. H.	35	20 c.c.	Ocular Palsy	GENERAL		NONE		NONE
4588	BRAIN	R. W.	22	10 c.c.	Epidural hematoma	LOCAL		NONE		NONE
92675	BRAIN	R. W.	41	30 c.c. (Done 4 days after, with Diodrast, 10 c.c. after 20 c.c. Dio.)	Meningioma	LOCAL & GENERAL	YES (20 c.c. in neck still visible after 24 days).	NONE	VOMITING	
6246	BRAIN	B. N.	73	20 c.c.	?	GENERAL		NONE		GOOD
6213	BRAIN	B. G.	17	40 c.c.	Epi-dural hematoma	GENERAL		NONE		GOOD
5713	BRAIN	B. F.	33	10 c.c. (after 20 c.c. of Dio. because urticaria)	Skull Fracture	GENERAL		NONE		
6388	BRAIN	G. S.	4	10 c.c.	Epilepsy	GENERAL	YES (10 c.c. in neck)	NONE		
23	1 - 22		1 to 79 years			12 GENERAL 11 LOCAL	7 extra-vascular injections.	0	4 VOMITING 4 CHILLS 1 SHOCK & CONVULSION	6 GOOD 1 VERY GOOD 4 POOR 2 NONE

Included in our series were 5 cases of intracranial hematoma, 1 case of bilateral carotid aneurysm, 2 cases of carotid thrombosis, 1 case of glioblastoma multiforme, 1 of meningioma and 1 of a skull metastasis from a hypernephroma. Fifty percent of these angiograms were done under general anaesthesia with Pentothal. General anaesthesia is used in children and in uncooperative patients; otherwise, we prefer to work under local anaesthesia only. We did not notice any reaction at the time of injection; we have the impression that the patients are not aware of

the exact time of the injection, which is impossible with the use of Diodrast. Delayed reactions, on the other hand, were more frequent with Angiopac. Four patients vomited, and these patients had not received Pentothal which might have explained the vomiting. Premedication though, with Demerol and sometimes hyoscine, could explain vomiting, at least partially. One patient had shock an hour after the angiogram but the examination had been done under general anaesthesia. A reaction peculiar to Angiopac or other colloidal substances, is shivering or chilling.

Four of our patients had a chill of at least half an hour's duration. This reaction subsided without medication each time. Such chills are not encountered with Diodrast. We are inclined to explain this shivering or tremor, which is a systemic reaction, by the mobilization of the reticulo-endothelial cells to phagocytose grains of Angiopac. None of our patients had a positive test prior to injection. (This would tend to eliminate the possibility of an allergic reaction.)

A new application of Angiopac is hepatosplenography, which is due to the accumulation of the dye in the liver and spleen after phagocytosis by the cells of the reticulo-endothelial system. Opacification of these organs occurs after 15 minutes and gradually disappears after the first hour.

After 13 of our angiograms, a scout film of

the abdomen was taken to see if the spleen and liver were opaque. This scout film was not taken with the exact technique or at the exact time prescribed for the optimum visualization of these organs; it was taken at the end of the examination just before the patient was returned to his room. In 11 of the 13 films there was dye accumulated in the spleen; this meant that we were able to draw the contours of the spleen much better than on a plain film. Four times, however, we considered this opacification to be unsatisfactory. Curiously, the dose administered did not seem to play a definite role in the degree of opacification. There may be, then, an individual factor due to the physiological response of the reticulo-endothelial system of each patient. This factor is undoubtedly difficult to analyze and we cannot attempt to do it now.

HEPATO-SPLENOGRAPHIES - with - ANGIOPAC

Table 2

NUMBER	NAME	AGE	DOSE	REACTION DURING INJECTION	REACTION AFTER INJECTION	FINAL DIAGNOSIS	OPACIFICATION OF LIVER	OPACIFICATION OF SPLEEN
4280	P. Y.	20	30 c.c.	None		Liver abscess	Poor	Very Good
4662	R. F.	20	30 c.c.	Sensation of heat		Thrombocytopenia	Poor	O (Splenectomy before) (Looking for aberrant spleen)
81490	B. R.	41	30 c.c.	Sensation of heat	Headache, fatigue, enlargement of lymphglands Rhinitis, lacrimation etc.	Chronic pancreatitis with Splenomegaly.	Poor	Good
5415	S. E.	40	30 c.c.	Sensation of heat	Chills	Splenomegaly	Poor	Good

Table 2 contains the important data concerning four patients upon whom a hepatosplenography or lienography has been attempted. The patients were two young adults and two older adults. The dose was 30 c.c. for each patient, injected intravenously. Three of the four patients noticed a sensation of generalized heat before the end of the injection. None of our angiogram patients complained of such a feeling, probably because only 10 c.c. were injected at a time, instead of 30 c.c. and perhaps because their attention was not directly attracted towards the injection and the possible reaction to it. The two young adults did not suffer from any late reaction, but the two older adults did. One of them had a chill exactly like the ones suffered by the other patients. The fourth had a very peculiar reaction: there was first a kind of allergic reaction, consisting of headache, fatigue, sensation of burning of the face, lacrimation and rhinitis. At the same time, an enlargement of almost all the lymph glands, which became very hard to palpation, was observed. The spleen, which was not palpable, became so for a time. The reaction

subsided within 24 hours. According to l'Union Chimique Belge, nobody else has observed such an enlargement of lymph glands. We suppose it could happen very easily, however, because of the colloidal nature of the product and its phagocytosis and accumulation in every organ where there are reticulo-endothelial cells.

Opacification of the liver was very poor in the four cases, but the spleen was well visualized in three patients. The fourth patient had had a previous splenectomy and we were looking for the possibility of aberrant spleen. This poor visualization of the liver might be overcome by a higher dose or by a more precise study of the optimum time of opacification.

It is not our intention to draw any conclusion from our experience, which is still too limited. We would like to state, however, that we have not yet had a serious reaction, although some were annoying to the patient. Should we continue to impose these annoying reactions on our patients? Priodax, for example, although accepted for cholecystography

has a high percentage of annoying reactions—nausea, vomiting, cramps and diarrhoea. Of course there are fewer indications for cerebral angiography and splenography than there are for cholecystography, and we must restrict these indications until we have the ultra-safe medium. We believe that Angiopac is less dangerous to the brain than Diodrast, as long as air embolism is avoided. We would be glad to use it extensively if it is proven safe enough, and for that reason it is our hope that every patient's reaction will be meticulously reported until we have a sufficient number of cases on which an opinion may be based. If

Angiopac is proven unsafe we shall search for another similar medium.

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REFRESHER COURSE ON MALIGNANT DISEASE

October 6th to 10th, 1952

British Columbia Cancer Institute

The official opening of the new building constructed by the British Columbia Cancer Foundation will be marked by a Refresher Course on Malignant Disease during the week of October 6th to 10th, 1952.

Principal speakers will be Sir Stanford Cade and Professor B. W. Windeyer of London, England. Also invited are Doctor Simeon T. Cantril and Doctor Franz Buschke of the Tumor Institute, Swedish Hospital, Seattle, Washington, Mr. H. M. Parker of Richland, Washington, and Doctor O. H. Warwick of Toronto.

ABDOMINAL AORTIC ANEURYSM

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The recognition of two abdominal aortic aneurysms in our department in January and February 1951, aroused my interest in the subject. In my student days we were taught that almost all aortic aneurysms were due to syphilis. Since that time however, more emphasis has been placed on the arteriosclerotic etiology.

A review of the better known articles on the subject brought forth the following facts:-

In 1903 Bryant¹ went through the records of Guy's Hospital, London, between 1854 and 1900 and discovered 325 cases of aortic aneurysm of which 54 or 16% were abdominal.

In 1905, Osler² reviewed 22,000 autopsies at Johns Hopkins, and found only 11 abdominal aortic aneurysms. He found that the ratio of abdominal to thoracic was 1:10.

In 1926, Oscar Klotz³ reviewed 1,000 aneurysms in Toronto and found 695 thoracic to 85 abdominal, that is 12.2% were abdominal. He believed the majority were due to syphilis but gave no figures.

Of the more recent series of cases, the most widely quoted is Kampmeier⁴, of New Orleans who reports 68 cases of abdominal aortic aneurysms, 57% of which were due to syphilis. However, only 20% of his cases were white. Almost 70% were under 45 years of age.

Hubeny and Pollack⁵ of Chicago, reported 48 cases, 74% of which were due to syphilis; 30% of them were white and the average age was in the 4th or 5th decade.

Scott⁷ of Johns Hopkins does not separate abdominal aortic aneurysms from aneurysms of the other large abdominal vessels. However, he found 21% were due to arteriosclerosis. He also noted that the average age for the luetic group was 30 to 39 and the arteriosclerotic group 60 to 69.

Mills and Horton⁸ of the Mayo Clinic reported 80 intra-abdominal aneurysms, 26 of which were aortic. Only 8.8% were syphilitic, only 1% were black and the age incidence was much older, 86% being over 51.

It was noted that males were more frequently affected than females. The different series showed 88% of Kampmeier's⁴, 80% of Hubeny and Pollack's⁵, 68% of Mills and Horton's⁸ and 85% of Scott's⁷ were males.

The age at which signs and symptoms become manifest varies according to etiology.

The average of appearance of syphilitic aortitis being 46.4 years and arteriosclerotic 72.7 years.

The location of the lesions also vary with etiology. Scott's⁷ figures show that almost all lesions above the renal arteries are luetic and below, 60% were arteriosclerotic.

Besides lues and arteriosclerosis a few other etiological factors are mentioned. A few abdominal aortic aneurysms of mycotic origin have been described. All these cases had endocarditis with haemolytic streptococcus as the causative organism.

Tuberculous glands breaking down in relation to the aorta have been described as causing aneurysms and one abdominal aneurysm as a result of a deep stab-wound is mentioned in the literature.

It might be wise to pause here and consider the anatomy of the abdominal aorta briefly. The aorta enters the abdomen at the level of the disc between T12 and L1. It lies in the mid-line on the bare vertebral column and ends at the level of the 4th lumbar body about $\frac{3}{4}$ of an inch below and to the left of the umbilicus by bifurcating into the right and left common iliacs. The aorta passes through the diaphragm by way of the lowermost of the three hiati at the T12-L1 disc. It is in relation to the crura laterally and the median arcuate ligament in front. The right crus is longer and stronger than the left. Microscopically the aorta has the usual three layers, intima, media and adventitia. The media contains the elastic elements which allow the aorta to dilate and contract with each cardiac pulsation. The wall is supplied by vasa vasorum which extend into the media.

Pathologically the changes in syphilis occur much more rapidly than in arteriosclerosis. They are due to a mesarteritis with patchy lymphatic infiltration about the vasa vasorum as they pass through the adventitia and media. They produce a marked scarring with early dilatation.

On the other hand arteriosclerosis produces gradual hyalinization of the media with loss of the elastic tissue. There is marked thickening and plaque formation. The plaques become calcified making x-ray visualization easier. The dilatation is slower but none the less progressive than the former type. The mechanics of aneurysm formation depends upon the principle that the pressure within a

segment of a vessel varies directly as the square root of the surface area. Therefore, the pressure is greatly increased within the sac which causes more dilatation which increases the pressure and thus the vicious circle continues.

From the clinical point of view, pain is the first subjective symptom. It may be constant, intermittent, dull or boring, sometimes it is described as throbbing. It may be in the epigastrium or back. If it radiates it is usually downward. The onset of pain usually heralds the beginning of the end. Kampmeier³ states that about 61% are dead within six months and 88% in one year after the onset of pain.

The most frequent finding is an abdominal mass more often to the left of the mid-line if high up. It usually manifests expansile pulsations. A bruit can be heard in about half the aneurysms. When the aneurysm ruptures a mass is usually present retroperitoneally unless it ruptures into the gastro-intestinal tract when haematemesis or melena are noted. We shall not try to differentiate between simple rupture and dissecting aneurysms in this paper.

Roentgenological studies of abdominal aortic aneurysms have followed the following patterns:—

- (a) Studies of the lower thoracic and lumbar spine usually comprising A.P. & Lateral views. According to the literature the most common finding is erosion of the bodies anteriorly. The discs are spared giving a scalloped appearance. The usual sites are T12 and L1 and 2. This is thought to be due to the restraining influence of the crura and median arcuate ligament of the diaphragm. This is also the site of luetic aneurysms being above the level of the renal arteries.
- (b) A flat plate of the abdomen may show nothing. If the aneurysm is large or is displacing gas-filled intestine it may be visible. If there is calcification in the wall of the aneurysm it can often be detected extending out from the side of the vertebral column. When this is noted a lateral view should be made because the aneurysms are always better visualized in them.
- (c) Gastro-intestinal studies can be done if the patient is not too ill. They serve to differentiate the mass from gastro-intestinal tract lesions and to delineate the mass with barium-filled viscera.
- (d) Intravenous pyelography serves to differentiate the mass from a renal lesion and to more accurately determine any displacement of the kidneys.
- (e) Pneumoperitoneum is useful in outlining the various abdominal structures and its use should be considered in a case where the diagnosis is difficult. We have had no experience with the procedure in cases of abdominal aneurysm.
- (f) Aortography has also been used but we have had no experience with this method of examination.

Case Reports

Case 1. Mr. N. R. white male, aged 74.

Was in his usual good health until six days prior to death when he developed bilateral low-back pain without radiation which lasted till death. Three days later he complained of a feeling of weakness, and during the afternoon he complained of a sharp tearing pain over the iliac crests which lasted a matter of minutes. He was admitted to hospital that day and was shocked and cyanotic when seen in the X-ray department where a chest film and flat film of the abdomen were made. The chest was not significant. The abdominal film showed a large mass on the right side obliterating liver, kidney and psoas shadows. The mass appeared to extend across to the left and could be seen extending beyond the 2nd, 3rd and 4th lumbar bodies for a distance of an inch or more. An X-ray diagnosis of possible ruptured aortic aneurysm was made at that time. On physical examination there was a firm mass with transmitted pulsation to the left and above the umbilicus. There was also marked tenderness in the left lower quadrant. On questioning, the patient admitted being aware of a pulsating mass in the upper abdomen for several months. Two days before death there was a recurrence of the sharp pain which was of short duration. The patient became progressively worse and died on January 18th, 1951. Post-mortem showed a massive retroperitoneal haemorrhage more marked on the right side. There was marked dilatation of the abdominal aorta over a length of 12 cms. arising 1.5 cms. below the region of the renal artery. There was a longitudinal defect 3 cms. long. The aneurysmal sac contained innumerable layers of old blood clot to a thickness of 1.5 cms. The remainder of the aorta showed marked atherosclerosis.

Case 2. Mr. G. I. white male, aged 24 years.

Gave a seven-month's history of vague lumbar pain. He was treated with an orthopaedic brace which gave relief. He also got relief by assuming a squatting position. Four days before death he experienced a sudden severe aching pain in the right side of his back just

above the iliac crest, and on the inner side of the right thigh. The pain was persistent and grew worse as time went on. It was associated with moderate diarrhoea. Physical examination revealed only an area of tenderness in the right lower quadrant. X-ray examination of the abdomen revealed a smooth soft tissue shadow with a convex lateral border to the right of the 2nd, 3rd and 4th lumbar vertebrae. The right kidney shadow was obliterated. It was felt that this was a retroperitoneal mass. No diagnosis was suggested. The patient was operated upon. An aneurysm was found in the upper abdominal aorta above the renal arteries. The aneurysm had ruptured. The patient died on the table. There was a large right-sided retroperitoneal hematoma. On pathological examination there was no evidence of syphilis and it was felt that this was a congenital aneurysm.

Case 3. Mr. B. H. a white male, aged 76.

Was admitted to hospital because of arteriosclerotic heart disease. His doctor reports that he has had auricular fibrillation for the past 4 years. He has had a backache for the past 3 years. It was not constant in intensity or location. It became worse just before admission and a diagnosis of arthritis of the lumbar spine was made clinically and X-rays were ordered to confirm this. These revealed a normal spine for a man of this age and an abdominal aortic aneurysm with calcification in the walls and a markedly calcified aorta above and below (Figure 1). A diagnosis of arteriosclerotic aneurysm was made. As far as is known the patient is still alive.



Fig. 1. A.P. and lateral of the lumbar spine show a large fusiform aneurysm opposite L3, 4 and 5 with no erosion of the vertebrae. The aneurysm is best seen in the lateral view and shows calcification in the walls.

Case 4. Mr. W. J. M. a white male, 54 years of age.

An apparently healthy robust man had been suffering from increasing low-back pain with referred pain over the course of the left

sciatic nerve. Spine films were made to investigate the cause of the pain and the calcified aortic aneurysm was discovered. He is still alive and his pain is no worse under conservative treatment.

Case 5. Mrs. E. B. a 78 year-old white female.

Was admitted with arteriosclerotic heart disease and cardiac failure. Chest films were made for heart size and a flat film was made of the abdomen. There was evidence of cardiac enlargement, bilateral pleural effusion and a large soft tissue mass extending from the left border of the 1st lumbar vertebra downwards and outwards, having a convex lateral border and ending at the 1st piece of the sacrum. The maximum convexity was at the 3rd lumbar vertebra where the lateral border is $4\frac{1}{2}$ cm. from the spine. There were areas of calcification in the wall of the mass and it was diagnosed as an aortic aneurysm (Figure 2). The patient died five months later of her heart disease without rupturing her aneurysm. No autopsy was obtained.



Fig. 2. An A.P. of the abdomen shows a large calcified aneurysm to the left of L2, 3, 4, and 5.

Case 6. Mr. J. P. a 74 year-old white male.

His chief complaint was shortness of breath for ten months before admission to hospital, in April of 1949. He was found to have

arteriosclerotic heart disease and idiopathic normochromic normocytic anaemia. The part of his story which was of interest to us was the fact that for at least two years he had noticed an expansile mass in the lower abdomen which was felt to beat with his heart. On physical examination an expansile mass with a palpable thrill and an audible systolic bruit was present in the right lower quadrant which was thought to extend up and across to the left side of the mid-line. Radiographs showed a mass to the right of the 4th and 5th lumbar vertebrae with calcification in the walls. A diagnosis of abdominal aortic aneurysm was made. His Wassermann was negative. In April, 1951, he was admitted because of hemoptysis and was found to have a pulmonary infarct. No films were made of the aorta at that time and no mention of enlargement was made. In July of 1951, he was again admitted because of increased fatigue and an increase in the size of his abdominal mass. Unfortunately through an oversight he was discharged without getting films of his abdomen. He died about a month later at home of cardiac failure without rupturing his aneurysm. No autopsy was obtained.

Case 7. Mrs. C. B. a white female aged 81.

She had a carcinoma of the body of the uterus. Films were made looking for bony metastases and an abdominal aortic aneurysm was found. Patient is still alive but her malignancy is considered inoperable.

Case 8. Mrs. J. R. 74 year-old white female.

Past history is that in 1934 she had a resection of her sigmoid colon for carcinoma. In 1939, she had a benign tumor removed from the right kidney. In 1944, a diaphragmatic hernia was repaired. She was in her usual good health until February 1951, when she noted a dull aching pain in the lower back. Two days later this radiated to the right flank and across the upper half of the abdomen. The patient vomited. The pain gradually subsided for a few days and then recurred. Physical examination showed a large pulsating mass in the right side of the abdomen. The peripheral vessels were arteriosclerotic. The Wassermann was negative. A.P. and oblique views of the abdomen showed a large mass extending to the right of the mid line. There was some calcification in the mass. An intravenous pyelogram showed the kidney to be distinct from the mass. A gastrointestinal series showed the mass to be displacing the stomach and duodenum upward and forward and the small bowel to the left. A diagnosis of abdominal aortic aneurysm was made and the patient was referred to the vascular surgery clinic.

Case 9. Mr. T. F. a 64 year-old white male.

Outside of a heart attack in 1946, the patient was in his usual good health until one day before death when he had several recurrent attacks of very severe left lower quadrant pain. He appeared shocked to his physician. There were no other physical findings except tenderness in the left lower quadrant. Throughout the day he became more shocked and the pain kept recurring. Three hours prior to death a mass could be outlined in the left lower quadrant. X-rays at this time showed a large soft tissue mass extending out from the mid-line to the left and obliterating the psoas shadow. There were also streaky areas of calcification on both sides of the vertebral column at the 4th and 5th lumbar suggestive of aneurysm. Consequently a ruptured aortic aneurysm was suggested. At autopsy there was an aneurysm measuring 12 x 9 cms. bulging to the right. It was situated between the renal artery and the bifurcation. There was a rent in the left side with massive retroperitoneal haemorrhage. Microscopic examination revealed arteriosclerosis with medial degeneration.

Case 10. Mr. C. B. a white male aged 68.

Was in his usual health until eight days before death when he experienced a sudden very sharp pain in the left lumbar region. He was admitted to hospital in shock and had tense muscles in left flank. He showed some improvement. Two days later he had another attack of pain and died. X-rays taken shortly after admission showed a large soft tissue mass on the left displacing the intestines to the right. No calcification could be seen. A ruptured abdominal aneurysm was suggested. Autopsy revealed a ruptured aneurysm of the lower aorta with retroperitoneal haemorrhage.

Case 11. Mrs. M. W. white female aged 67.

She had pain in the left lower quadrant for four days, and nausea and vomiting for two days before death. X-rays showed a left paravertebral mass with calcification along the border. At autopsy there was a ruptured sacular arteriosclerotic abdominal aneurysm below the renal arteries. There was a massive haemorrhage.

Mr. W. C. a white male aged 60.

Two days before death he had a sudden onset of acute left-sided epigastric pain not relieved by morphine. This was followed by five loose bowel movements. On examination a smooth mass was noted in the left upper quadrant with abdominal distension. An X-ray of the abdomen showed calcification on the

left side of L1 suggestive of an aortic aneurysm. There was a soft tissue mass in the left side obliterating kidney and psoas shadow and the stomach was displaced to the right. A diagnosis of ruptured aortic aneurysm was made. At post-mortem there was rupture of an aortic aneurysm with massive retroperitoneal haemorrhage.

Case 13. Mrs. C. V. C. a white female aged 65.

Slipped and strained the muscles of her abdominal wall. Was sent in by her doctor for urinary tract films, which showed a calcified shadow extending out from her vertebral column. This suggested aortic aneurysm, so a lateral was made and the patient was examined. She had a pulsating mass in the mid-abdomen which was expansile. The films were typical of an arteriosclerotic abdominal aortic aneurysm.

Conclusions:

Our small series of 13 cases show twelve arteriosclerotic and one congenital aneurysm and no luetic ones. With the exception of the congenital one, who was 24 years old, the average age of our group was 69.5. All were white. All the aneurysms were below the renal arteries and none showed erosion of the verte-

brae. At the present time, six have died of their aortic disease, two have died of other causes, and five are still alive. Our series resembled the one reported from the Mayo Clinic⁵ of 26 cases in which only 1% were black and only 8.8% were luetic, more closely than the others where syphilis was more common. With the decline in the prevalence of syphilis and an increase in the average age of our patients, we can expect to see more arteriosclerotic aneurysms. It is more important for us to be able to diagnose them in view of the hope of cure held out by improved vascular surgery.

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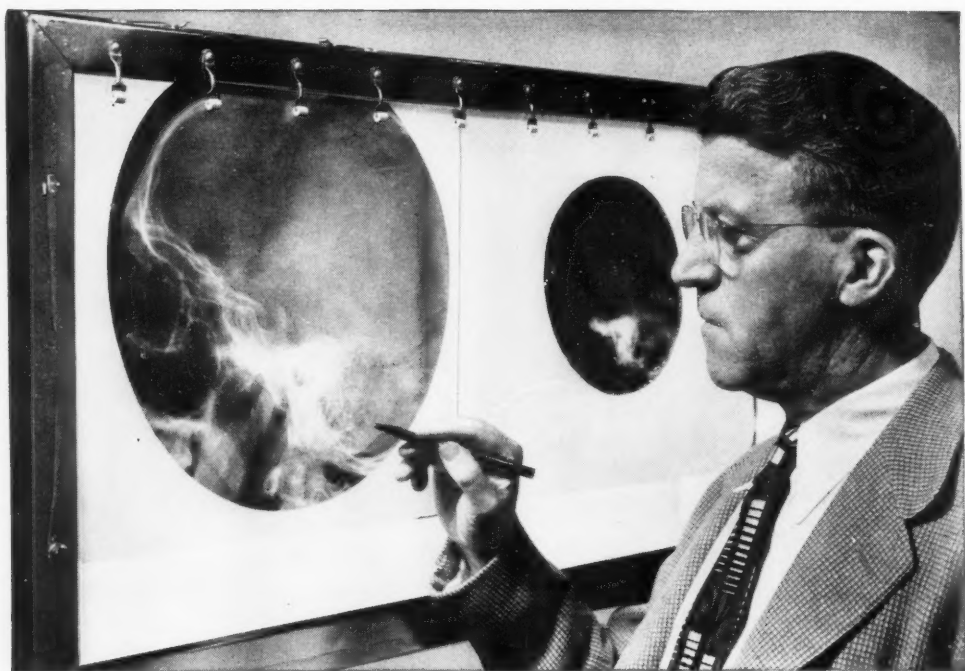
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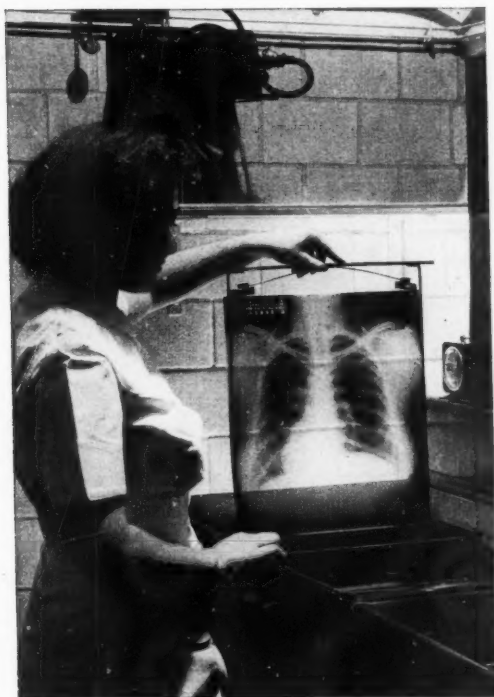
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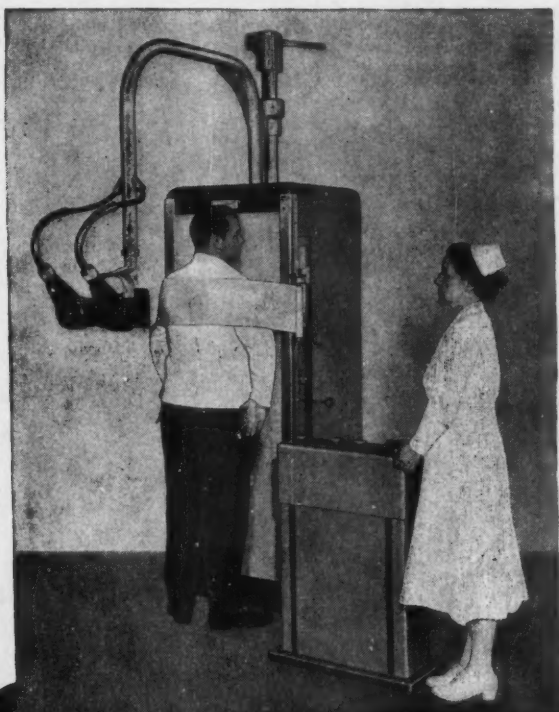
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